General

Guideline Title

Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America.

Bibliographic Source(s)

Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, Raad II, Rolston KV, Young JA, Wingard JR. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis. 2011 Feb;52(4):e56-93. [337 references] PubMed

Guideline Status

This is the most current release of the guideline.

This guideline updates a previous version: Hughes WT, Armstrong D, Bodey GP, Bow EJ, Brown AE, Calandra T, Feld R, Pizzo PA, Rolston KV, Shenep JL, Young LS. 2002 guidelines for the use of antimicrobial agents in neutropenic patients with cancer. Clin Infect Dis 2002 Mar 15;34(6):730-51. [191 references]

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 12, 2016 – Fluoroquinolone Antibacterial Drugs : The U.S. Food and Drug Administration (FDA) is advising that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.
- January 4, 2016 – Noxafil (posaconazole) : The U.S. Food and Drug Administration (FDA) is cautioning that differences in dosing regimens between the two oral formulations of the antifungal Noxafil (posaconazole) have resulted in dosing errors. To help prevent additional medication errors, the drug labels were revised to indicate that the two oral formulations cannot be directly substituted for each other but require a change in dose. Direct mg for mg substitution of the two formulations can result in drug levels that are lower or higher than needed to effectively treat certain fungal infections.

Recommendations

Major Recommendations

Quality of evidence (I–III) and strength of recommendation (A–C) ratings are defined at the end of the "Major Recommendations" field.

What Is the Role of Risk Assessment and What Distinguishes High-Risk and Low-Risk Patients with Fever and Neutropenia?

1. Assessment of risk for complications of severe infection should be undertaken at presentation of fever (A-II). Risk assessment may determine the type of empirical antibiotic therapy (oral vs. intravenous [IV]), venue of treatment (inpatient vs. outpatient), and duration of antibiotic therapy (A-II).
2. Most experts consider high-risk patients to be those with anticipated prolonged (>7 days duration) and profound neutropenia (absolute neutrophil count [ANC] ≤100 cells/mm^3 following cytotoxic chemotherapy) and/or significant medical co-morbid conditions, including hypotension, pneumonia, new-onset abdominal pain, or neurologic changes. Such patients should be initially admitted to the hospital for empirical therapy (A-II).
3. Low-risk patients, including those with anticipated brief (≤7 days duration) neutropenic periods or no or few comorbidities, are candidates for oral empirical therapy (A-II).
4. Formal risk classification may be performed using the Multinational Association for Supportive Care in Cancer (MASCC) scoring system (B-I).
    i. High-risk patients have a MASCC score <21 (B-I). All patients at high risk by MASCC or by clinical criteria should be initially admitted to the hospital for empirical antibiotic therapy if they are not already inpatients (B-I).
    ii. Low-risk patients have a MASCC score ≥21 (B-I). Carefully selected low-risk patients may be candidates for oral and/or outpatient empirical antibiotic therapy (B-I).

What Specific Tests and Cultures Should be Performed during the Initial Assessment?

5. Laboratory tests should include a complete blood cell (CBC) count with differential leukocyte count and platelet count; measurement of serum levels of creatinine and blood urea nitrogen; and measurement of electrolytes, hepatic transaminase enzymes, and total bilirubin (A-III).
6. At least 2 sets of blood cultures are recommended, with a set collected simultaneously from each lumen of an existing central venous catheter (CVC), if present, and from a peripheral vein site; 2 blood culture sets from separate venipunctures should be sent if no central catheter is present (A-III). Blood culture volumes should be limited to <1% of total blood volume (usually ~70 mL/kg) in patients weighing <40 kg (C-III).
7. Culture specimens from other sites of suspected infection should be obtained as clinically indicated (A-III).
8. A chest radiograph is indicated for patients with respiratory signs or symptoms (A-III).

In Febrile Patients With Neutropenia, What Empiric Antibiotic Therapy Is Appropriate and in What Venue?

9. High-risk patients require hospitalization for IV empirical antibiotic therapy; monotherapy with an anti-pseudomonal beta-lactam agent, such as cefepime, a carbapenem (meropenem or imipenem-cilastatin), or piperacillin-tazobactam, is recommended (A-I). Other antimicrobials (aminoglycosides, fluoroquinolones, and/or vancomycin) may be added to the initial regimen for management of complications (e.g., hypotension and pneumonia) or if antimicrobial resistance is suspected or proven (B-III).
10. Vancomycin (or other agents active against aerobic gram-positive cocci) is not recommended as a standard part of the initial antibiotic regimen for fever and neutropenia (A-I). These agents should be considered for specific clinical indications, including suspected catheter-related infection, skin or soft-tissue infection, pneumonia, or hemodynamic instability.
11. Modifications to initial empirical therapy may be considered for patients at risk for infection with the following antibiotic-resistant organisms, particularly if the patient's condition is unstable or if the patient has positive blood culture results suspicious for resistant bacteria (B-III). These include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococcus (VRE), extended-spectrum beta-lactamase (ESBL)–producing gram-negative bacteria, and carbapenemase-producing organisms, including *Klebsiella pneumoniae* carbapenemase (KPC). Risk factors include previous infection or colonization with the organism and treatment in a hospital with high rates of endemicity.
    i. MRSA: Consider early addition of vancomycin, linezolid, or daptomycin (B-III).
    ii. VRE: Consider early addition of linezolid or daptomycin (B-III).
    iii. ESBLs: Consider early use of a carbapenem (B-III).
    iv. KPCs: Consider early use of polymyxin-colistin or tigecycline (C-III).

12. Most penicillin-allergic patients tolerate cephalosporins, but those with a history of an immediate-type hypersensitivity reaction (e.g., hives and bronchospasm) should be treated with a combination that avoids beta-lactams and carbapenems, such as ciprofloxacin plus clindamycin or aztreonam plus vancomycin (A-II).
13. Afebrile neutropenic patients who have new signs or symptoms suggestive of infection should be evaluated and treated as high-risk patients (B-III).
14. Low-risk patients should receive initial oral or IV empirical antibiotic doses in a clinic or hospital setting; they may be transitioned to outpatient oral or IV treatment if they meet specific clinical criteria (A-I).
    i. Ciprofloxacin plus amoxicillin-clavulanate in combination is recommended for oral empirical treatment (A-I). Other oral regimens, including levofloxacin or ciprofloxacin monotherapy or ciprofloxacin plus clindamycin, are less well studied but are commonly used (B-III).
    ii. Patients receiving fluoroquinolone prophylaxis should not receive oral empirical therapy with a fluoroquinolone (A-III).
    iii. Hospital re-admission or continued stay in the hospital is required for persistent fever or signs and symptoms of worsening infection (A-III).

When and How Should Antimicrobials be Modified During the Course of Fever and Neutropenia?

15. Modifications to the initial antibiotic regimen should be guided by clinical and microbiologic data (A-II).
16. Unexplained persistent fever in a patient whose condition is otherwise stable rarely requires an empirical change to the initial antibiotic regimen. If an infection is identified, antibiotics should be adjusted accordingly (A-I).
17. Documented clinical and/or microbiological infections should be treated with antibiotics appropriate for the site and for the susceptibilities of any isolated organisms (A-I).
18. If vancomycin or other coverage for gram-positive organisms was started initially, it may be stopped after 2 days if there is no evidence for a gram-positive infection (A-II).
19. Patients who remain hemodynamically unstable after initial doses with standard agents for neutropenic fever should have their antimicrobial regimen broadened to include coverage for resistant gram-negative, gram-positive, and anaerobic bacteria and fungi (A-III).
20. Low-risk patients who have initiated IV or oral antibiotics in the hospital may have their treatment approach simplified if they are clinically stable (A-I).
    i. An IV-to-oral switch in antibiotic regimen may be made if patients are clinically stable and gastrointestinal absorption is felt to be adequate (A-I).
    ii. Selected hospitalized patients who meet criteria for being at low risk may be transitioned to the outpatient setting to receive either IV or oral antibiotics, as long as adequate daily follow-up is ensured (B-III). If fever persists or recurs within 48 hours in outpatients, hospital re-admission is recommended, with management as for high-risk patients (A-III).

21. Empirical antifungal coverage should be considered in high-risk patients who have persistent fever after 4–7 days of a broad-spectrum antibacterial regimen and no identified fever source (A-II).

How Long Should Empirical Antibiotic Therapy be Given?

22. In patients with clinically or microbiologically documented infections, the duration of therapy is dictated by the particular organism and site; appropriate antibiotics should continue for at least the duration of neutropenia (until ANC is $\geq$500 cells/mm^3) or longer if clinically necessary (B-III).
23. In patients with unexplained fever, it is recommended that the initial regimen be continued until there are clear signs of marrow recovery; the traditional endpoint is an increasing ANC that exceeds 500 cells/mm^3 (B-II).
24. Alternatively, if an appropriate treatment course has been completed and all signs and symptoms of a documented infection have resolved, patients who remain neutropenic may resume oral fluoroquinolone prophylaxis until marrow recovery (C-III).

When Should Antibiotic Prophylaxis be Given, and With What Agents?

25. Fluoroquinolone prophylaxis should be considered for high-risk patients with expected durations of prolonged and profound neutropenia (ANC $\leq$100 cells/mm^3 for >7 days) (B-I). Levofloxacin and ciprofloxacin have been evaluated most comprehensively and are considered to be roughly equivalent, although levofloxacin is preferred in situations with increased risk for oral mucositis-related invasive viridans group streptococcal infection. A systematic strategy for monitoring the development of fluoroquinolone resistance among gram-negative bacilli is recommended (A-II).
26. Addition of a gram-positive active agent to fluoroquinolone prophylaxis is generally not recommended (A-I).
27. Antibacterial prophylaxis is not routinely recommended for low-risk patients who are anticipated to remain neutropenic for <7 days (A-III).

What Is the Role of Empirical or Pre-emptive Antifungal Therapy and Which Antifungal Should be Used?

High Risk

28. Empirical antifungal therapy and investigation for invasive fungal infections should be considered for patients with persistent or recurrent fever after 4–7 days of antibiotics and whose overall duration of neutropenia is expected to be >7 days (A-I). Data are insufficient to recommend a specific empirical antifungal agent for a patient already receiving anti-mold prophylaxis, but switching to a different class of anti-mold antifungal that is given intravenously should be considered (B-III).
29. Preemptive antifungal management is acceptable as an alternative to empirical antifungal therapy in a subset of high-risk neutropenic patients. Those who remain febrile after 4–7 days of broad-spectrum antibiotics but are clinically stable, have no clinical or chest and sinus computed tomography (CT) signs of fungal infection, have negative serologic assay results for evidence of invasive fungal infection, and have no recovery of fungi (such as *Candida* or *Aspergillus* species) from any body site may have antifungal agents withheld (B-II). Antifungal therapy should be instituted if any of these indicators of possible invasive fungal infection are identified.

Low Risk

30. In low-risk patients, the risk of invasive fungal infection is low, and therefore routine use of empirical antifungal therapy is not recommended (A-III).

When Should Antifungal Prophylaxis be Given and With What Agents?

High Risk

31. Prophylaxis against *Candida* infection is recommended in patient groups in whom the risk of invasive candidal infection is substantial, such as allogeneic hematopoietic stem cell transplant (HSCT) recipients or those undergoing intensive remission-induction or salvage-induction chemotherapy for acute leukemia (A-I). Fluconazole, itraconazole, voriconazole, posaconazole, micafungin, and caspofungin are all acceptable alternatives.
32. Prophylaxis against invasive *Aspergillus* infections with posaconazole should be considered for selected patients ≥13 years of age who are undergoing intensive chemotherapy for acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) in whom the risk of invasive aspergillosis without prophylaxis is substantial (B-I).
33. Prophylaxis against *Aspergillus* infection in pre-engraftment allogeneic or autologous transplant recipients has not been shown to be efficacious. However, a mold-active agent is recommended in patients with prior invasive aspergillosis (A-III), anticipated prolonged neutropenic periods of at least 2 weeks (C-III), or a prolonged period of neutropenia immediately prior to HSCT (C-III).

Low Risk

34. Antifungal prophylaxis is not recommended for patients in whom the anticipated duration of neutropenia is <7 days (A-III).

What Is the Role of Antiviral Prophylaxis and What Virus Infections Require Antiviral Treatment?

35. Herpes simplex virus (HSV)–seropositive patients undergoing allogeneic HSCT or leukemia induction therapy should receive acyclovir antiviral prophylaxis (A-I).
36. Antiviral treatment for HSV or varicella-zoster virus (VZV) infection is only indicated if there is clinical or laboratory evidence of active viral disease (C-III).
37. Respiratory virus testing (including testing for influenza, parainfluenza, adenovirus, respiratory syncytial virus [RSV], and human metapneumovirus) and chest radiography are indicated for patients with upper respiratory symptoms (e.g., coryza) and/or cough (B-III).
38. Yearly influenza vaccination with inactivated vaccine is recommended for all patients being treated for cancer (A-II). Optimal timing of vaccination is not established, but serologic responses may be best between chemotherapy cycles (>7 days after the last treatment) or >2 weeks before chemotherapy starts (B-III).
39. Influenza virus infection should be treated with neuraminidase inhibitors if the infecting strain is susceptible (A-II). In the setting of an influenza exposure or outbreak, neutropenic patients presenting with influenza-like illness should receive treatment empirically (C-III).
40. Routine treatment of RSV infection in neutropenic patients with upper respiratory disease should not be given (B-III).

What Is the Role of Hematopoietic Growth Factors (G-CSF or GM-CSF) in Managing Fever and Neutropenia?

41. Prophylactic use of myeloid colony-stimulating factors (CSFs; also referred to as hematopoietic growth factors) should be considered for patients in whom the anticipated risk of fever and neutropenia is ≥20% (A-II).
42. CSFs are not generally recommended for treatment of established fever and neutropenia (B-II).

How are Catheter-Related Infections Diagnosed and Managed in Neutropenic Patients?

43. Differential time to positivity (DTP) >120 min of qualitative blood cultures performed on specimens simultaneously drawn from the CVC and a vein suggests a central line–associated blood stream infection (CLABSI) (A-II).
44. For CLABSI caused by *S. aureus*, *Pseudomonas aeruginosa*, fungi, or mycobacteria, catheter removal is recommended in addition to systemic antimicrobial therapy for at least 14 days (A-II). Catheter removal is also recommended for tunnel infection or port pocket site infection, septic thrombosis, endocarditis, sepsis with hemodynamic instability, or bloodstream infection that persists despite ≥72 hours of therapy with appropriate antibiotics (A-II).
45. For documented CLABSI caused by coagulase-negative staphylococci, the catheter may be retained using systemic therapy with or without antibiotic lock therapy (B-III).
46. Prolonged treatment (4–6 weeks) is recommended for complicated CLABSI, defined as the presence of deep tissue infection, endocarditis, septic thrombosis (A-II) or persistent bacteremia or fungemia occurring >72 hours after catheter removal in a patient who has received appropriate antimicrobials (A-II for *S. aureus*, C-III for other pathogens).
47. Hand hygiene, maximal sterile barrier precautions, and cutaneous antisepsis with chlorhexidine during CVC insertion are recommended for all CVC insertions (A-I).

What Environmental Precautions Should be Taken When Managing Febrile Neutropenic Patients?

48. Hand hygiene is the most effective means of preventing transmission of infection in the hospital (A-II).
49. Standard barrier precautions should be followed for all patients, and infection-specific isolation should be used for patients with certain signs or symptoms (A-III).
50. HSCT recipients should be placed in private (i.e., single-patient) rooms (B-III). Allogeneic HSCT recipients should be placed in rooms with >12 air exchanges/hour and high-efficiency particulate air (HEPA) filtration (A-III).
51. Plants and dried or fresh flowers should not be allowed in the rooms of hospitalized neutropenic patients (B-III).
52. Hospital work exclusion policies should be designed to encourage health care workers (HCWs) to report their illnesses or exposures (A-II).

Definitions:

Strength of Recommendation*

A. Good evidence to support a recommendation for or against use.
B. Moderate evidence to support a recommendation for or against use.
C. Poor evidence to support a recommendation.

Quality of Evidence*

I. Evidence from ≥1 properly randomized, controlled trial.
II. Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments.
III. Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

*Adapted from Canadian Task Force on the Periodic Health Examination, 1979. Reproduced with the permission of the Minister of Public Works and Government Services Canada.

Clinical Algorithm(s)

Clinical algorithms are provided for the following:

- Initial management of fever and neutropenia
- Reassess after 2-4 days of empirical antibiotic therapy
- High-risk patient with fever after 4 days of empirical antibiotics

Scope

Disease/Condition(s)

Disease/Condition(s)

Cancer chemotherapy-induced fever and neutropenia

Note: *Fever* is defined as a single oral temperature of >38.3° C (101° F); or ≥38.0° C (100.4° F) for ≥1 hour. *Neutropenia* is defined as an absolute neutrophil count (ANC) <500/mm^3 or an ANC that is expected to decrease to <500 cells/mm^3 during the next 48 hours.

Guideline Category

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Critical Care

Family Practice

Hematology

Infectious Diseases

Internal Medicine

Oncology

Pediatrics

Preventive Medicine

Intended Users

Advanced Practice Nurses

Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

- To assist practitioners in making decisions about appropriate care for neutropenic patients who present with signs and symptoms of potentially serious infections
- To provide a guide for the use of antimicrobial agents in managing patients with cancer who experience chemotherapy-induced fever and neutropenia
- To provide a clearer definition of which populations of patients with cancer may benefit most from antibiotic, antifungal, and antiviral prophylaxis

Target Population

Patients with cancer who experience chemotherapy-induced fever and neutropenia

Interventions and Practices Considered

Diagnosis/Evaluation

1. Risk assessment (Multinational Association for Supportive Care in Cancer [MASCC] scoring system)
2. Laboratory test
    - Complete blood cell (CBC) count with differential leukocyte and platelet count
    - Blood chemistry (creatinine and blood urea nitrogen; and measurement of electrolytes, hepatic transaminase enzymes, and total bilirubin)
    - Blood cultures
    - Culture specimens from other sites as clinically indicated
    - Chest radiograph as indicated

Management/Treatment

1. Empirical antibiotic therapy (monotherapy with an anti-pseudomonal beta-lactam agent, such as cefepime, a carbapenem (meropenem or imipenem-cilastatin), or piperacillin-tazobactam)
2. Other antimicrobials (aminoglycosides, fluoroquinolones, and/or vancomycin)
3. Modifications to antibiotic therapy during the course of fever and neutropenia
    - Methicillin-resistant *Staphylococcus aureus* (MRSA) (addition of vancomycin, linezolid, or daptomycin)
    - Vancomycin-resistant enterococcus (addition of linezolid or daptomycin)
    - Extended-spectrum beta-lactamase (ESBL)-producing gram-negative bacteria (carbapenem)
    - Klebsiella pneumoniae carbapenemase (KPC)-resistant bacteria (polymyxin-colistin or tigecycline)
4. Avoidance of beta-lactams and carbapenems in penicillin-allergic patients
5. Duration of therapy
6. Empirical antifungal therapy as indicated
7. Management of central line-associated bloodstream infections

Prevention

1. Antibiotic prophylaxis according to risk stratification
2. Antifungal prophylaxis (fluconazole, itraconazole, voriconazole, posaconazole, micafungin, and caspofungin) according to risk stratification
3. Antiviral prophylaxis (acyclovir) according to risk stratification
4. Hematopoietic growth factors
    - Granulocyte-colony stimulating factor (G-CSF)
    - Granulocyte macrophage-colony stimulating factor (GM-CSF)
5. Environmental precautions
    - Hand hygiene
    - Barrier precautions
    - Private hospital room
    - High-energy particulate air filtration
    - Avoid dried or fresh flowers
    - Hospital work exclusion policies

Major Outcomes Considered

- Multinational Association for Supportive Care in Cancer risk-index score
- Requirement for empiric antibiotic and/or antifungal therapy
- Drug-related adverse effects
- Development of drug-resistant organisms
- Secondary infection(s)

- Morbidity and mortality
- Cost of treatment

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

For the 2010 update, the Panel completed the review and analysis of data published since 2002. Computerized literature searches of the PUBMED database were performed. The searches of the English-language literature from 2002 through July 2009 combined the terms "ANTIBIOTICS" and "FEVER" and "NEUTROPENIA." Data published after July 2009 were also considered in the final preparation of the manuscript. The searches were limited to human-only studies and to specific study design or publication type: clinical trial, randomized clinical trial, meta-analysis, or practice guideline.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence*

I. Evidence from ≥1 properly randomized, controlled trial.
II. Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments.
III. Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

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Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

In evaluating the evidence regarding the management of patients with fever and neutropenia, the Panel used a systematic weighting of the level and grade of the evidence for making a recommendation (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee reconvened many members of the original guideline panel, together with additional experts in the management of patients with fever and neutropenia. The Panel included experts in infectious diseases, oncology, and hematopoietic stem cell transplant (HSCT) in both adult and pediatric patients.

The Panel met on >10 occasions via teleconference (including subgroup calls) and once in person to complete the work of the guideline. The purpose of the teleconferences was to discuss the questions, distribute writing assignments, and finalize recommendations. All members of the Panel participated in the preparation and review of the draft guideline.

The recommendations are derived from well-tested patterns of clinical practice that have emerged from cancer therapy clinical trials; modifications of these recommendations are based upon careful review of data from recent scientific publications and peer-reviewed information whenever possible. When evidence-based recommendations cannot be made because of insufficient data, the Panel has provided guidance that is based on the consensus of its members, all of whom have extensive experience in the treatment of neutropenic patients.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation*

A. Good evidence to support a recommendation for or against use.
B. Moderate evidence to support a recommendation for or against use.
C. Poor evidence to support a recommendation.

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Cost Analysis

The guideline developers reviewed published cost-analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Feedback from external peer reviews was obtained. The guideline was reviewed and approved by the Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee and the Board of Directors prior to dissemination.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified with each recommendation (see "Major Recommendations").

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management and treatment of cancer patients with fever and neutropenia

Potential Harms

- Drug-related adverse effects
- Development of drug-resistant organisms

Contraindications

Contraindications

The use of rectal thermometers, enemas, suppositories, and rectal examinations is contraindicated for patients with neutropenia.

Qualifying Statements

Qualifying Statements

- It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. The Infectious Diseases Society of America considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.
- These guidelines were developed in the context of North American practices. Some recommendations may not be as applicable outside of North America, in areas where differences in available antibiotics, in the predominant pathogens, and/or in health care–associated economic conditions exist.
- The definitions of fever and neutropenia in this guideline are general criteria that should be used to identify patients in whom empirical antibiotic therapy must be initiated. However, these definitions are not hard-and-fast rules. Clinical variations among patients mandate that clinical judgment play a critical role in identifying which patients require antibiotics during the risk period of neutropenia, even if those patients do not meet these specific definitions.
- During fever and neutropenia, no specific drug or combination of drugs and no specific period of treatment can be unequivocally recommended for all patients. Rather, the recommendations outlined in these guidelines are generally applicable in most clinical situations but, in some instances, will require modifications according to circumstances and local epidemiologic data.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Mobile Device Resources

Pocket Guide/Reference Cards

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, Raad II, Rolston KV, Young JA, Wingard JR. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis. 2011 Feb;52(4):e56-93. [337 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1997 Sep (revised 2011 Feb)

Guideline Developer(s)

Infectious Diseases Society of America - Medical Specialty Society

Source(s) of Funding

Infectious Diseases Society of America (IDSA)

Guideline Committee

Composition of Group That Authored the Guideline

Panel Members: Alison G. Freifeld, Department of Medicine, University of Nebraska Medical Center, Omaha, Nebraska; Eric J. Bow, Departments of Medical Microbiology and Internal Medicine, the University of Manitoba, and Infection Control Services, Cancer Care Manitoba, Winnipeg, Manitoba, Canada; Kent A. Sepkowitz, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York; Michael J. Boeckh, Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research, Seattle, Washington; James I. Ito, Division of Infectious Diseases, City of Hope National Medical Center, Duarte, California; Craig A. Mullen, Department of Pediatrics, University of Rochester Medical Center, Rochester, New York; Issam I. Raad, Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas M.D. Anderson Cancer Center, Houston, Texas; Kenneth V. Rolston, Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas M.D. Anderson Cancer Center, Houston, Texas; Jo-Anne H. Young, Department of Medicine, University of Minnesota, Minneapolis, Minnesota and John R. Wingard, Division of Hematology/Oncology, University of Florida, Gainesville, Florida

Financial Disclosures/Conflicts of Interest

All members of the Panel complied with the Infectious Diseases Society of America (IDSA) policy on conflicts of interest, which requires disclosure of any financial or other interest that might be construed as constituting an actual, potential, or apparent conflict. Members of the Panel completed the IDSA conflict of interest disclosure statement and were asked to identify ties to companies developing products that might be affected by promulgation of the guideline. Information was requested regarding employment, consultancies, stock ownership, honoraria, research funding, expert testimony, and membership on company advisory committees. The Panel made decisions on a case-by-case basis as to whether an individual's role should be limited as a result of a conflict. No limiting conflicts were identified.

Potential Conflicts of Interest: A.G.F. is a member of the advisory panel for the National Comprehensive Cancer Network Guidelines for "Prevention and Treatment of Infections in Patients with Cancer"; has received research support from Merck, Pfizer, Enzon, Astellas, and Chimerix; and has served as a consultant to Enzon. M.J.B. has received research support from Roche Laboratories, ViroPharma, Vical, Novartis, and Arrow Therapeutics; has served as a consultant to ViroPharma, Roche Laboratories, Novartis, and AiCuris; and has given lectures for Roche and Pfizer. I.I.R. has received grants from Cubist, Schering-Plough, Versicor, Enzon, Astellas Pharma US, Pfizer, Cook, and Wyeth; has served on the speakers' bureau of Merck, Pfizer, and Cook; and has received royalties related to patents licensed to Cook, Akorn, American Medical Systems, Horizon Medical Products, and Tyrx as a co-inventor. J.I.I. has received honoraria from Astellas, Enzon, Pfizer, Schering-Plough (now Merck), and Cubist and serves as an advisor to Enzon. J.H.Y. has served on the speakers' bureaus of Schering-Plough, Astellas Pharma, and Pfizer; has served as a consultant to Merck and Schering-Plough; and has conducted clinical trials for Schering-Plough, Astellas Pharma, Pfizer, Merck, and ViroPharma. J.R.W. has received honoraria from Merck, Pfizer, Astellas, and Schering-Plough and has served as a consultant to Pfizer, Merck, Astellas, Basilea, and Nektar. K.V.R. has served as a consultant to Astellas and received research grants from Cubist, Astellas, and Merck. E.J.B. has received honoraria from Merck-Frosst, Pfizer, Astellas, and Schering-Plough and has served as a consultant to Pfizer, Merck-Frosst, Astellas, Amgen, and Wyeth. All other authors: no conflicts.

Guideline Status

This is the most current release of the guideline.

This guideline updates a previous version: Hughes WT, Armstrong D, Bodey GP, Bow EJ, Brown AE, Calandra T, Feld R, Pizzo PA, Rolston KV, Shenep JL, Young LS. 2002 guidelines for the use of antimicrobial agents in neutropenic patients with cancer. Clin Infect Dis 2002 Mar 15;34(6):730-51. [191 references]

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Infectious Diseases Society of America (IDSA) Web site .

Print copies: Alison G. Freifeld, MD, Immunocompromised Host Program, Dept of Medicine, University of Nebraska Medical Center, Omaha, NE 68198-5400 (afreifeld@unmc.edu).

Availability of Companion Documents

The following are available:

- Fever and neutropenia in cancer patients. Pocket guide. Infectious Diseases Society of America (IDSA); 2011. 16 p. Electronic copies: Available from the Infectious Diseases Society of America (IDSA) Web site .
- A version of the guideline for mobile devices is available from the Infectious Diseases Society of America (IDSA) Web site .

In addition, performance measures are available in the original guideline document .

Patient Resources

None available

NGC Status

This summary was completed by ECRI on January 15, 1999. The information was verified by the guideline developer as of March 22, 1999. This summary was updated on June 10, 2002. The updated information was verified by the guideline developer as of June 18, 2002. This NGC summary was updated by ECRI Institute on April 1, 2011. The updated information was verified by the guideline developer on May 11, 2011. This summary was updated by ECRI Institute on November 22, 2011 following the U.S. Food and Drug Administration (FDA) advisory on Zyvox (linezolid). This summary was updated by ECRI Institute on September 10, 2012 following the U.S. Food and Drug Administration advisory on Cefepime. This summary was updated by ECRI Institute on October 24, 2013 following the U.S. Food and Drug Administration advisory on Tygacil (tigecycline). This summary was updated by ECRI Institute on October 25, 2013 following the U.S. Food and Drug Administration advisory on Fluoroquinolone Antibacterial Drugs. This summary was updated by ECRI Institute on March 6, 2014 following the U.S. Food and Drug Administration advisory on Over-the-Counter Topical Antiseptic Products. This summary was updated by ECRI Institute on January 6, 2016 following the U.S. Food and Drug Administration advisory on Noxafil (posaconazole). This summary was updated by ECRI Institute on May 18, 2016 following the U.S. Food and Drug Administration advisory on Fluoroquinolone Antibacterial Drugs.

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